Remarks

Rejection Under 35 U.S.C. § 102

Claims 102, 105, 108, 112, 114, 117, 118, 120, 122, 133, 135, and 136 were rejected under 35 U.S.C. § 102(a) as being anticipated by Reszka, et al., J. Pharmacology and Experimental Therapeutics 280(1): 232-237 (1/1997) ("Reszka") or Beck, et al., Microencapsulation 10(1):101-114 (1993) ("Beck"). Applicants respectfully traverse these rejections to the extent that it is applied to the claims as amended.

Claim 102 has been amended to delete poloxamer 188 from the Markush group and to correct a grammatical error.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987).

a. Reszka

Reszka describes the use of three compositions: (1) liposomes; (2) polybutylcyanoacrylate (PBCA) nanoparticle which were prepared by emulsion polymerization using 1% butylcyanoacrylate monomer, 1% dextran 70 and 0.2% polyoxamer 188 in 0.01 N HCl; and (3) PBCA nanoparticles coated with 1% poloxamine, loaded with an active agent, mitoxantrone, for treatment of melanomas. Reszka, however, does not disclose nanoparticles **consisting essentially** of a polymeric material

comprising one or more monomeric or oligomeric precursors polymerized in the presence of one or more stabilizers, and loaded with one or more physiologically effective substances to be delivered to the central nervous system, wherein the one or more stabilizers are chosen from the Markush group defined in claim 102. The applicants do not claim the use of dextran 70 or poloxamer 188 as suitable stabilizers for delivering an active agent to the central nervous system. Note, although the word "comprising" is used, it refers to the polymer forming the nanoparticle and therefore **cannot** include a separate coating step. Accordingly, claims 102, 105, 108, 112, 114, 117, 118, 120, 122, 133, 135, and 136 are not anticipated by Reszka.

b. Beck

Beck describes the use of three compositions: (1) liposomes; (2) polybutylcyanoacrylate (PBCA) nanoparticle which were prepared by emulsion polymerization using 1% butylcyanoacrylate monomer, 1% dextran 70 and 0.2% polyoxamer 188 in 0.01 N HCl; and (3) PBCA nanoparticles coated with 1% poloxamine, loaded with an active agent, mitoxantrone, for treatment of melanomas. Beck, however, does not disclose nanoparticles **consisting essentially** of a polymeric material comprising one or more monomeric or oligomeric precursors polymerized in the presence of one or more stabilizers, and loaded with one or more physiologically effective substances to be delivered to the central nervous system, wherein the one or more stabilizers are chosen from the Markush group defined in claim 102. The applicants do not claim the use of

dextran 70 or poloxamer 188 as suitable stabilizers for delivering an active agent to the central nervous system. Accordingly, claims 102, 105, 108, 112, 114, 117, 118, 120, 122, 133, 135, and 136 are not anticipated by Beck.

Rejection Under 35 U.S.C. § 103

Claims 102, 105, 108, 112, 114, 117, 118, 120, 122, 133, 135, and 136 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Reszka or Beck, in view of WO 95/22963 to Kreuter ("Kreuter"). Applicants respectfully traverse these rejections to the extent that it is applied to the claims as amended.

Claim 102 has been amended to delete poloxamer 188 from the Markush group and to correct a grammatical error.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference or references must teach or suggest all claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Kreuter discloses that treatment of nanoparticles having a drug absorbed, adsorbed or incorporated therein with a sufficient ***coating*** of an appropriate surfactant

allows the adsorbed drug to traverse the bbb (page 6, lines 13-15). Kreuter describes the preparation of PBCA nanoparticles using an acidic polymerization medium containing dextran 70000 as a stabilizer (page 14, lines 18-20). After polymerization, the nanoparticles were loaded with the drug to be delivered. Finally, the nanoparticles were coated by the addition of a 1% solution of surfactant, preferably Polysorbate 80, to the nanoparticle suspension (page 7, lines 15-17). Kreuter does not disclose or suggest the use of stabilizers other than dextran 70.

As discussed above, Reszka and Beck describe the use of three compositions: (1) liposomes; (2) polybutylcyanoacrylate (PBCA) nanoparticle which were prepared by emulsion polymerization using 1% butylcyanoacrylate monomer, 1% dextran 70 and 0.2% polyoxamer 188 in 0.01 N HCl; and (3) PBCA nanoparticles coated with 1% poloxamine, loaded with an active agent, mitoxantrone, for treatment of melanomas. However, neither Reszka or Beck discloses nanoparticles consisting essentially of a polymeric material comprising one or more monomeric or oligomeric precursors polymerized in the presence of one or more stabilizers, and loaded with one or more physiologically effective substances to be delivered to the central nervous system wherein the one or more stabilizers are chosen from the Markush group defined in claim 102. Reszka and Beck do not disclose or suggest the use of any other stabilizers besides dextran 70 and poloxamer 188. Importantly, Beck discloses that the ***surfactant coating***

appears to influence the efficacy of nanoparticles, and as such, other coatings besides poloxamine 1508 should be investigated.

Therefore, one of ordinary skill in the art would not be motivated to combine the teachings of Kreuter, Reszka and Beck to prepare nanoparticles consisting essentially of a polymeric material comprising one or more monomeric or oligomeric precursors polymerized in the presence of one or more stabilizers, and loaded with one or more physiologically effective substances to be delivered to the central nervous system, wherein the one or more stabilizers are chosen from the Markush group defined in claim 102.

Allowance of claims 102, 105, 108, 112, 114, 117, 118, 120, 122, 133, 135, and 136 is respectfully solicited.

Respectfully submitted,

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